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# Multiple Ependymomas in a Patient With Turcot's Syndrome

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A 21-year-old woman was diagnosed with Turcot's syndrome (TS) at age 16 years. She had two ependymomas, one was located in the left middle cerebellar peduncle and the other in the low sacral spinal canal. Her mother and brother both had colectomies for colonic polyposis. Her maternal uncle and grandfather also had this disease and both died from cancer of the colon in their fourth decade of life.

The patient was found to have hyperpigmented spots in the retina, skull osteomas and normal neurological examinations. The bone scan and CSF were normal and she had a germline mutation in the segment 3 of the adenomatous polyposis coli (APC) gene. Following partial resection of the two ependymomas, she was treated with radiation and chemotherapy.

One year after surgery, paraspinal desmoid tumors were found and removed. She is presently 42 months postsurgical resection of the neural tumors and has remained central nervous system tumor-free. The occurrence of multiple ependymoma in TS has not been reported, and the control of this patient's ependymomas is consistent with other reports of long-term survival with TS and glial tumors.



**Key words:** Turcot's syndrome, multiple ependymomas, desmoid tumors

## INTRODUCTION

Turcot's syndrome (TS) is a rare autosomal dominant inherited disorder, which includes the presence of multiple colorectal adenomas and primary malignancies of the central nervous system (CNS). Medulloblastoma and glioblastoma multiforme are the most common primary CNS tumors reported in patients with TS [1]. Ependymoma has been reported in one case [2]. Multiple sites of CNS tumors have been rarely noted in TS, but none have involved ependymomas [3].

Patients with familial adenomatous colonic polyposis (FACP) are at high risk to develop carcinoma of the colon, extracolonic cancers and soft tissue tumors, such as desmoids [4,5] Desmoid tumors are found in 10% of patients with FACP and they commonly develop after trauma or abdominal surgery. The peritoneal wall and mesenteric tissue are the usual locations [6].

We present a young woman with TS, who developed two ependymomas and paraspinal desmoids tumors. This case is unusual because multiple ependymomas and paraspinal desmoids have not been reported in patients with TS.

## CASE

A 16-year-old Hispanic girl sought medical attention for pain in the right leg and ankle for several weeks. She had no history of headaches, dizziness, weakness, sensory symptoms, or bladder and bowel dysfunction.

At 4 years of age, she was found to have hyperpigmented spots in the right retina and skull osteomas. At age 9 years, she had partial colectomy to treat colonic polyposis. Her mother and brother have both had colectomies for colonic polyposis. Her maternal uncle and grandfather also had colonic polyposis and both died of cancer of the colon in their fourth decade of life. The patient had normal neurological examinations, except for limping with the right leg.

MRI scans showed two tumors, one located in the left cerebellar pontine angle and the other in the lower sacral spinal canal (Figs. 1, 2). Bone scan was normal and CSF was negative for malignant cells.

Partial resection of both tumors was performed. The cerebellar tumor was anaplastic ependymoma and the sacral tumor was reported as a mixopapillary ependymoma. She received radiation therapy with 3,600 cGy to the posterior fossa and entire spinal axis and with a total of 5,580 cGy to both tumor beds. Chemotherapy included vincristine and cisplatin which was given concomitant with radiation therapy, and followed with three cycles of ifosphamide, carboplatin and etoposide.

One year after surgery, she developed pain in the right lumbosacral paraspinal area, weakness in the right leg and increasing difficulty in walking. She had tender subcutaneous masses in the lumbosacral and thoracic areas and weakness of the extensors and flexors of the right hip and quadriceps femoris muscles. MRI showed tumors

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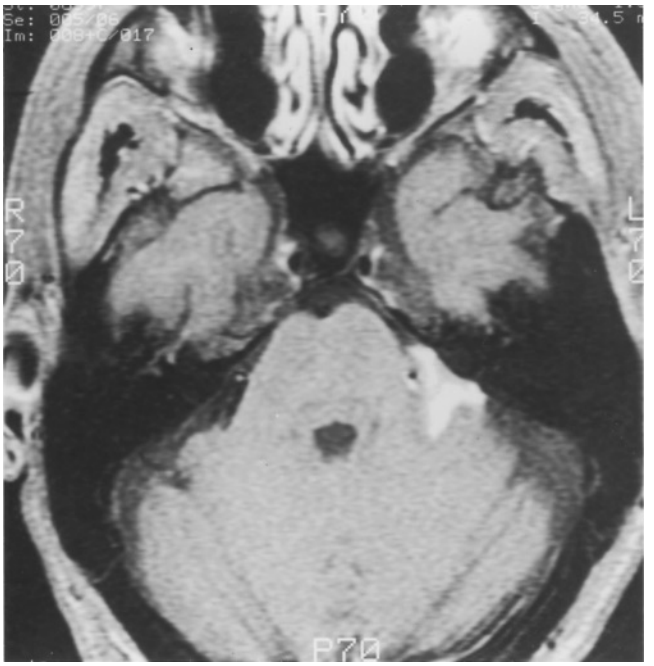

**Fig. 1.** MRI T1-weighted image with gadolinium injection. A homogenous enhancing mass is noted in the left pontocerebellar angle with minimal edema around the tumor.

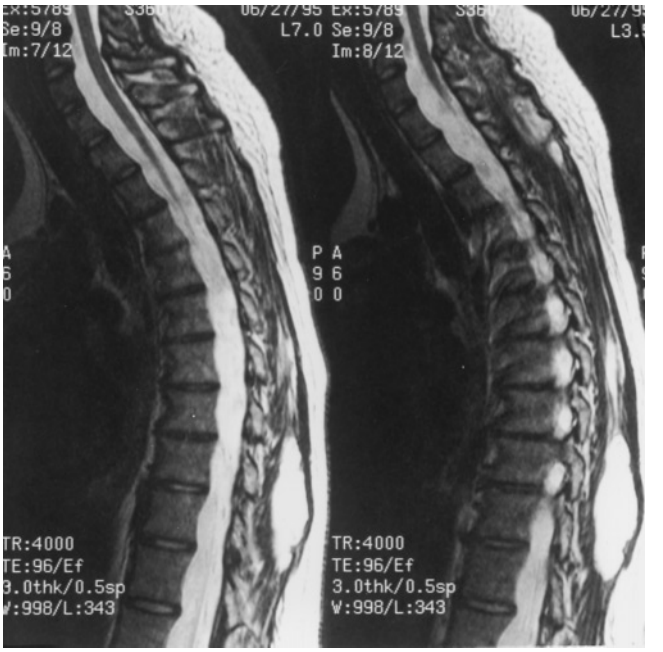


**Fig. 3.** MRI of the thoracic spine. A large subcutaneous mass is seen in the thoracic paraspinal level. The mass is hyperintense in the T2-weighted image.

**Fig. 2.** MRI of the lumbosacral spine. T1-weighted image with gadolinium injection shows an irregular mass with low intensity signal in the center, consistent with necrosis and surrounding enhancing tissue.

in the right and left paraspinal regions with mild enhancement to gadolinium injection (Fig. 3). Gross total resection was performed and the tumors were reported as desmoids, tumors without signs of malignancy. Following surgery, the patient's symptoms and signs improved considerably. Over the last year, however, she has developed another large subcutaneous lump in the left upper thoracic, paraspinal area. MRI has shown a large, mass with identical findings to those of desmoid tumors. Follow-up surveillance MRIs of the brain and spine have shown no evidence of CNS tumor relapse.

## DISCUSSION

Turcot's syndrome has been reported in association with FACP and with hereditary, nonpolyposis colorectal cancer. The genetic abnormality in these two disorders has been recently identified [2,7] and the gene for FAPC has been mapped to chromosome 5q 21. The FACP is associated with a germ-line mutation of the APC gene and the nonpolyposis colorectal cancer with a mutation of a mismatch-repair gene. Both syndromes have autosomal dominant inheritance. The phenotype characteristics of these two disorders can be indistinguishable. The nonpolyposis colorectal cancer patients usually have few, if any, precancer colonic symptoms.

The average age of patients with FACP at the time of diagnosis of CNS tumor is earlier (18.2 y) than the average age of FACP patients with colon-rectal carcinoma (39 y) [3,8]; therefore, some young patients with TS (FACP and CNS tumor) may not have a family history suggestive of TS.

In an extensive review of the medical literature, symptoms of brain tumor were present before the diagnosis of

polyposis in 71% of TS cases [8]. Patients with FACP have a higher risk of developing CNS tumor than the normal population. This risk is 23 times higher among the group from birth to 29 years and by a factor of 7 in all age group [2]. The relative risk of cerebellar medulloblastoma in patients with FACP was found to be 92 times higher than in the general population [2]. The risk for developing brain tumors in patients with nonpolyposis colorectal cancer is unknown.

The majority of TS patients with primary brain tumors have medulloblastoma, anaplastic astrocytoma or glioblastoma multiforme. In a study by Hamilton et al. [2] medulloblastoma was the predominant brain tumor associated with the mutation of the germ-line APC gene, and glioblastoma multiforme was found in patients with mutations in the mismatch-repair gene. Ependymoma has been reported in one instance [2] but multiple CNS ependymomas have not been previously reported in patients with TS.

Multiple adenomatous polyps in the colon are also seen in the Gardner's syndrome (GS). This syndrome also includes benign osteomas, sebaceous cysts, desmoid tumors and tumors of other soft tissues. Hyperpigmented lesions in the retina have been found in 90% of patients with GS [9]. This syndrome, however, unlike TS does not include CNS tumors [7]. The present case has abnormal hyperpigmentation of the retina, benign skull osteomas and desmoid tumors. These data add to the hypothesis that TS, GS and FACP are genetically related.

The 5-year free disease-free survival of children with infratentorial ependymomas without TS has been reported as 30–35%. Long-term CNS disease-free survival in patients with TS and CNS tumors has been observed but no clear explanation for this occurrence has been offered [10]. The present patient has remained CNS tumor-free 42 months after partial resection, 40 months after radiation, and 32 months out of chemotherapy.

Desmoid tumors arise from soft tissue and sometimes can be aggressive. They can invade the muscles, tendons and other tissues in the vicinity. They do not metastasize and surgery will usually control their growth. They also respond to radiation and chemotherapy. In the present case, the desmoid tumors in the lumbosacral area have not relapsed following surgery. Because glioblastoma multiforme is a more aggressive tumor and less responsive to therapy than medulloblastoma, genetic analysis has been suggested to help with the proper classification and prognosis. The molecular genetic analysis in the present case showed germ-line mutation of the adenomatous polyposis coli (APC) gene. Whether the favorable response of this patient's tumors to therapy is related to this type of gene mutation remains unknown.

Patients with colonic polyposis presenting with signs or symptoms suggesting a neurological disorder should have prompt and careful neurological investigation, including a MRI scan. Early awareness that families with colonic polyposis are at high risk for developing brain tumors may lead to earlier diagnosis and higher cure rates of CNS tumors that have high morbidity and mortality.

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